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Book Reviews

Handbook of Pharmaceutical Analysis. Lena Ohannesian and Anthony J. Streeter, Eds., Marcel Dekker, Inc., New York, New York, 2002. xii, 585 pp., illustrations. $195.00.

This long overdue revision to previous edition (Pharmaceutical Analysis: Modern Methods [in two parts], edited by James W. Munson) is still oriented to filling the gap between undergraduate texts and detailed monographs and reviews. The editors and their contributing authors have endeavored to provide broad overviews of a number of topics of interest to pharmaceutical analysts, with extensive references to the primary peer-reviewed literature. Many of the chapters in the present edition provide updated coverage of topics reviewed in the original edition, including high performance liquid chromatography, ultraviolet-visible spectrophotometry, atomic spectroscopy, and luminescence spectroscopy. Chapters on thin-layer chromatography, gas chromatography and functional group analysis have been dropped from this revision.

The chapter on mass spectrometry surveys modern implementations of this technique, with a thorough discussion of the different ionization modes now in use and some discussion of new interfacing methods. The remainder of the chapter discusses application of mass spectrometry to metabolism studies. The chapter on capillary electrophoresis emphasizes both its application to the study of traditional small molecule active pharmaceutical ingredients as well as the role played by this technology in advancing the science of genomics. Capillary electrophoresis and microchip analogs are the method of choice for polynucleotide research. The chapter on immunoassay techniques surveys not only the many variants of this technology in use today, but also briefly describes and evaluates the many approaches to data analysis for binding assays, which may challenge the thinking of analysts schooled in traditional calibration curve based methods. The very extensive literature review of immunoassay methods is especially valuable. To employ any of the analytical techniques described in the other chapters, samples must first be prepared for analysis. The chapter on sample preparation describes many of the challenges facing the analyst.

Three chapters emphasize analytical methods appropriate to characterizing solid forms of drugs. The book starts off with a primer on polymorph screening, properties of hydrated forms and salt selection. An overview of appropriate analytical methods is given with a discussion of how each technique described can be applied to characterizing a pharmaceutical solid. This chapter also gives step by step approaches to selecting an appropriate solid form for the active pharmaceutical ingredient. The chapter on solid state nuclear magnetic resonance spectroscopy complements this introduction. The chapter on vibrational spectroscopy (infrared and Raman methods) is also largely devoted to solid state characterization. These three chapters together provide a comprehensive overview of methods appropriate for characterizing pharmaceutical solids. Anyone charged with the responsibility of characterizing pharmaceutical active ingredients or for specifying the final solid form will find these chapters invaluable.

The book concludes with a chapter on statistical considerations in pharmaceutical process development and validation. Pharmaceutical analysis today is concerned primarily with the measurement of properties of active pharmaceutical ingredients, excipients, and finished drug dosage forms to assure the quality of the final marketed product. Although estimation of the average properties of the test substance is still important, the focus of most quality control measurements is the estimation of variation, an art in which classically trained pharmaceutical analysts have seldom been educated. The final chapter emphasizes statistically justifiable approaches to the measurement of variability, with examples from blend uniformity testing, determination of particle size distributions, considerations in unit dose sampling, the use of control charts to identify batch differences, evaluation of process capability, and setting realistic specifications. Estimation of process variability based on actual measured properties is stressed, contrary to outmoded practices based on inadequate data as specified in compendia such as the U.S.P. To illustrate, the section on setting specifications demonstrates as one approach the use of statistical tolerance intervals; the abbreviated table of tolerance factors given assumes that you have as a minimum seven replicate measurements on which to base your projection and clearly illustrates the advantage of choosing a more reasonable number (for example, 20). Unless you have just won the Iron Man triathlon, your heart isn't strong enough to stand the sight of the tolerance factors needed if you have only two or three replicates on which to base your decision; the author has kindly spared you. The implications for assay precision validation experiments are mind-boggling. The only unfortunate omission in the final chapter is a failure to point out clearly that the analytical system used to evaluate product quality is itself a process, and that the assessment of process capability necessarily includes contributions to the overall variability both from the manufacturing process and the analytical process used to study it. Nevertheless, if you read no other part of this book than the final chapter and apply some of the practices recommended, it will have paid for itself.

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Combinatorial Library Design and Evaluation. Principles, Software Tools, and Applications in Drug Discovery. Arup K. Ghose and Vellarkad N. Viswandhan, Eds., Marcel Dekker, Inc., New York, New York, 2001. xv, 631 pp., illustrations. $195.00.

A full realization of the power of combinatorial chemistry for drug design is critically dependent on appropriate design of the most relevant libraries of compounds. The editors

and authors of this book have succeeded in providing an excellent introduction to current theory and methodology that is pertinent to the rational design of these combinatorial libraries.

The book is divided into four sections, the first being an introductory chapter focused on chemical aspects of combinatorial library design and implementation. The second section, on design principles, provides six chapters encompassing subject areas such as pharmacophore modeling, quantitative structure activity relationships (QSAR) and 3D-QSAR, molecular docking, electrostatics methodologies, and integration of pharmacokinetics and binding affinity. The third section, on current methods and software tools, extends the basic principles described in the second section into eight chapters focused on current algorithms and software. The final section of the book comprises five chapters on applications of combinatorial library design.

Whereas this book is clearly focused on the rational design of combinatorial libraries in drug discovery, it also provides an excellent compendium of available methodologies for QSAR, 3D-QSAR, and other aspects of structure-function analysis. As a result it should be of particular interest to medicinal chemists and others seeking to solve problems of diversity vs. similarity in combinatorial library design, but it will also be helpful to those medicinal and pharmaceutical chemists, peptide and protein chemists, computational chemists and biochemists, and pharmacologists who are studying structure-activity-relationships independent of combinatorial chemistry. The fifty authors from both industrial and academic settings have provided chapters that are clear and well organized with ample references to previous primary and secondary literature. The somewhat brief index is complemented by chapter titles and subheadings that have sufficient information for the reader to quickly and efficiently navigate through the text for specific topics. Overall, this book provides an excellent compilation and explanation of the many approaches available for the rational design of combinatorial libraries for drug discovery.

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Drug-Drug Interactions. A. David Rodrigues, Ed., Marcel Dekker, Inc., New York, New York, 2002. xviii, 650 pp., illustrations. $195.00.

Drug-drug interactions are an important cause of attrition in preclinical and clinical drug development, and one of the worrying causes of adverse drug reactions in pharmacotherapy. To grasp the size of the latter problem, just recall the report (*Journal of the American Medical Association*, April 13, 1998) showing that over 100,000 hospitalized patients died in 1994 from severe reactions to drugs in the USA, and another 2.2 millions were seriously injured. Of course drug-drug interactions do not account for all adverse drugs reactions, but they often play a contributing or even predominant role. A book presenting an up-to-date, systematic and comprehensive account of the various aspects of drug-drug interactions would therefore be more than welcome. Despite its merits, the present book falls short of meeting such an expectation.

Drug-drug interactions can be of a pharmacokinetic (PK) or a pharmacodynamic (PD) nature. Pharmacodynamic interactions occur at sites of drug action (e.g., receptors), and they can be additive, synergistic or antagonistic, as aptly explained by Rowland in the introductory chapter. Because the outcome of such PD interactions is often predictable, they seldom pose a problem in pharmacotherapy. Understandably, the main body of *Drug-Drug Interactions* is exclusively concerned with pharmacokinetic drug-drug interactions. This renders all the more valuable the concluding chapters (Chapters 15–18) on the clinical, toxicological, regulatory and marketing perspectives of pharmacokinetic drug-drug interactions. Here, their pharmacodynamic consequences are discussed in a broader medicinal context.

Chapters 2–14 cover various aspects of pharmacokinetic drug-drug interactions, but do so without any apparent connection and logic in their sequence. Thus, two chapters (5 and 8) are dedicated to the fast developing field of interactions at the level of transporters. Various important aspects of interactions at the level of the CYP enzymes are covered in Chapters 3 (a broad overview), 6 (in vitro models), 10 (inhibition), and 12 (in vivo probes). Other important aspects are discussed in chapters intertwined with these, namely UDPGT (Chapter 4), *in vitro* approaches for identifying responsible enzymes (7), the role of the gut mucosa (9), prediction of metabolic drug interactions (Chapter 11), molecular modeling (Chapter 13) and the presentation of a metabolic drug interaction database (Chapter 14). All these chapters make for instructive and stimulating reading, although their incorporation into a fragmented and unordered coverage has left this reader somewhat frustrated. What one misses, indeed, is a more systematic and coherent picture, one that would aim at educating readers by integrating concepts, methods, sites and mechanisms.

It is inevitable in a book of this nature that there should be some overlap between chapters, but this is in fact a useful feature as it allows readers to see links and create their own synthetic understanding. Less commendable, perhaps, is the fact that one chapter (Chapter 13) shows an unusual degree of homology with two previous writings by the same team, one under the same copyright, the other not.

Technically, the book was well produced. Its presentation is clear and the artwork of uniform good quality. The bibliography is rich and up-to-date, and it includes titles and full pagination. There is also a subject index. In summary, this is a useful book for many facts and diverse viewpoints it contains.

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Drug Targeting Technology, Physical, Chemical, Biologic Methods. Drugs and the Pharmaceutical Sciences Volume 115, Hans Schreier, Ed., Marcel Dekker, Inc., New York, New York, 2001, x, 597 pp., illustrations. $150.00.

As mentioned by the editor, the aim of the book is to serve as an eye opener for interested professionals and students, open for lateral views beyond the boundaries of their own fields of interest. It is not intended to be an exhaustive anthology of drug targeting techniques and strategies, but rather a highlight on the diversity of approaches in drug delivery. It is therefore divided into three sections. The first ("physical") deals with oral and pulmonary formulations, as well as methods to enhance drug accumulation in the lymphatic system and penetration enhancement through the skin. The second section ("chemical") deals with the soft pro-drug approach and recognition methods to direct drugs to the liver. The third section contains short chapters on gene delivery with liposomes containing viral proteins ("artificial viral envelopes") and specific promoters in gene therapy.

The first chapter deals with enteric coating technologies allowing safe passage of solid dosage forms through the stomach into the small intestine, *in vitro* assessments and some applications. Colonic delivery systems are reviewed by Kurt Bauer who provides a comprehensive review on the various methods used to ferry drugs into the large intestine. Pulmonary delivery is next in turn. The chapter summarizes some particulate delivery systems used to localize steroid drugs in the lungs and lists pharmacokinetic considerations in their design and highlights pharmacokinetic and pharmacodynamic aspects. An excellent review was written by Porter and Charman on lipid-based formulations to facilitate drug absorption into the lymphatic compartment after oral administration. It focuses on physicochemical and biochemical means for increasing bioavailability. A chapter on various methods to enhance drug permeation through the skin concentrates on flexible polymer and liposomal systems. This chapter also presents a variety of penetration enhancers used in transdermal delivery.

Retrometabolic design is mentioned in the context of soft prodrug approach to direct drugs to diseased tissues. A special attention is paid to the blood brain barrier and its penetration by soft prodrugs. A typical example is the "lock-in" mechanism for estradiol derivatives. An interesting section is the one, which deals with neoglyco- and neopeptide albumins for targeting hepatocytes. After a profound physiological preface, it reviews critical aspects of the conjugation concept in targeting to the liver. The last part of the book selectively concentrates on some gene delivery techniques using liposomes containing viral binding proteins and on targeting cancer cells with viral vectors differentiating between tissue-specific, endothelium-specific and tumor-selective promoters.

One of the goals of the editor was to provide a feel for the necessity to combine micro and macro technologies to accomplish feasible targeting. However, the inexperienced reader will find it difficult to navigate among the various sections of the book, which appear to lack a solid cord to fulfill this mission.

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Controlled Release Veterinary Drug Delivery: Biologic and Pharmaceutical Considerations. Michael J. Rathbone and Robert Gurny, Eds., Elsevier Science B.V., Amsterdam, the Netherlands, 2000. xvi, 375 pp., illustrations. $207.00.

This book is organized into 13 chapters and gives a very good overview of the applications of controlled release technologies in the veterinary field. The editors and their coauthors have provided information describing both livestock and companion animal uses covering a variety of routes of administration. They have included chapters on testing procedures, stability testing, and USA regulatory aspects of controlled release technology. (They were unable to find an author to present the EU and Japanese regulatory perspective on controlled release technology). There is an informative chapter detailing the pharmacokinetic and biopharmaceutical principles that need to be considered in the development of a livestock or companion animal product. The chapter describing mechanisms of drug release from veterinary delivery systems provides insight into the large number of drug delivery systems that have been developed using simple to complex technologies. This chapter should be a basic introduction for every formulator designing controlled drug delivery systems. Knowledge of the release mechanism provides insight to the formulator in the rational design and optimization of drug release from the delivery system. The chapters summarizing intraruminal, rumen stable, post-ruminal, ocular, and intravaginal veterinary delivery systems are detailed and up to date. The chapters reviewing drug delivery systems for estrous control and control of ectoparasites of livestock provide a detailed synopsis of the field. Additional chapters provide the status of controlled release vaccines in veterinary medicine and a review of controlled release products for companion animals. The book should be required reading for all formulators working on veterinary applications of controlled release and will provide insight to those developing controlled release drug delivery technologies into the wide variety of potential applications that exist in veterinary medicine.

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Dermatological and Transdermal Formulations. Kenneth A. Walters, Ed., Marcel Dekker, Inc., New York, New York, 2002. x, 567 pp., illustrations. $195.00.

The preface acknowledges the original Marcel Dekker volume written by Brian Barry '*Dermatological Formulations–*

Percutaneous Absorption' and it is not surprising that there are many similarities in the structure of the two books. Brian Barry was the sole author of the manuscript, which has served for over two decades as a major reference text in the subject of skin permeation. Many of the basic issues remain the same but research into the mechanisms of percutaneous absorption has progressed and this is reflected in the multi-authored contributions that form the basis of Walters' book. In Barry's book there were 7 chapters covering the field. Of these only the final chapter, that on rheology, is not covered in the new text. The 6 additional chapters reflect different aspects of the subject and are a useful addition to a reference text. The book starts with a traditional review of the structure and function of the skin and also introduces biochemical elements of barrier maintenance. Repair mechanisms and damage are given brief coverage.

It should be recognized that a large percentage of the population suffers from some form of dermatological disorder and that 25% of these should receive medical intervention. The impact that skin disorders has on the quality of life is profound and it is interesting to see that chapter 3 does address common skin disorders and their treatment. Obviously this is a huge subject but the review highlights the depth of the problem and the medical aspect is a useful addition to the overall text. To design topical and transdermal agents so that they are more effective it is important to understand the physicochemical determinants that control membrane transport. This was covered very well in Barry's original book but this chapter does include some newer evaluations of Fick's laws of diffusion. There is a constant reminder (equation 33, chapter 2) that it is very easy to miss typographical errors and it is also difficult to compare equations 81 and 82 with 83 since the latter is in the Laplace domain.

The meat of the book is in the next 3 chapters. Skin transport is covered very comprehensively with 332 references. It reviews many aspects objectively including the route of penetration and the role of partition and solubility. Partition processes are discussed on the basis of chemical potential and the problems associated with an indiscriminate use of concentration and thermodynamic activity are avoided. This leads on to structure activity relationships, always useful when trying to predict permeation rates of novel compounds. The chapter then goes on to develop the role of skin-vehicle-drug interactions, concepts that were introduced by the pioneering work of Katz and Poulsen in the '60's. To determine the concentration of the active at the site of action it is important to understand the rate of delivery and the clearance kinetics. The importance of skin pharmacokinetics is addressed and significance of the different clearance processes discussed. In vitro-in vivo correlations are briefly mentioned at the conclusion of the chapter. The second chapter in this trilogy examines the methods for studying percutaneous absorption. Since Barry's works there have been numerous workshops—symposia addressing the regulatory aspects of both *in vitro* and *in vivo* techniques for assessing percutaneous absorption. This chapter reviews the different approaches. It considers the standard issues such as cell design, receptor phase, membrane preparation etc. It also introduces the problems of skin metabolism. *In vivo* experimentation covers intact animal models, skin flaps and grafts. With recent developments in tissue culture and the use of cultured skin for assessing various aspects of penetration, metabolism and toxicity I would have liked to see greater coverage of this topic. Skin stripping has been used to good effect in the past and again recent developments have demonstrated the significance of the technology, the most recent of these have presumably not been covered because of the gestational age of any textbook of this nature. As in the previous chapter it ends with a discussion of *in vivo–in vitro* correlations and the two complement each other. As is well known the skin is a very effective barrier and to deliver as much active agent as possible enhancement strategies are often adopted. The final chapter of the three considers a number of ways of improving delivery. These include a representative selection of chemical enhancers, supersaturation (building on the concepts of chemical potential described in Chapter 4) and vesicles such as conventional liposomes and Transfersomes. The problem of inadvertent supersaturation during product manufacture is also described. What is perhaps surprising is that throughout the text there is little mention of physical mechanisms of promoting absorption an area that has developed considerably since Barry's definitive text.

The following chapter is an overview of topical formulations such as ointments, gels, and emulsions and develops into regulatory issues concerning drug release from these semisolid matrices. It would have been interesting to see a discussion of design approaches to topical formulations using the physical chemistry of chapters 3 and 4 as a fundamental basis. The design of transdermal systems is covered in brief and this is followed by a review of the clinical use of those drugs that have been approved for transdermal use.

One of the major problems with topical medicines is the inability to measure the bioavailability of the active at the site of action. This is highlighted in an excellent chapter entitled 'Bioavailability of Dermatologicals'. It is written by practitioners in the area and includes important issues such as dose titration, a subject that is often forgotten or ignored in topical therapy. The review explains the differences between different 'equivalencies' (pharmaceutical, biopharmaceutical, and therapeutic), often a minefield in topical products or transdermal system submissions to the regulatory authorities. A range of examples is given and emphasis is given to statistical issues, both *in vitro* and *in vivo* models, and vehicle effects. The chapter is very well referenced.

The final three chapters are brief résumés covering issues of scale up, safety considerations, and transdermal delivery and cutaneous reactions. There are elements of similarity between the penultimate and the final chapter but the two are complementary. Many companies have developed transdermal systems in the past only to find that the active shows some evidence of skin toxicity. This is an important issue in the development of patches that will reside on the skin for extended periods of time. The two chapters help to identify the particular problems involved in this area and how they may be investigated in a rational way.

This is an important reference text that builds on the original work of Brian Barry. It will find a place particularly, I feel, for research workers in the pharmaceutical industry and academic research supervisors working on topical products. With the increasing potency of medicinal agents it is important to design the formulations so that they have the opportunity of dose titration. I feel that the book could have placed more emphasis on the rational design of topical and transdermal drugs and how they can be formulated from first

principles. The book is very well referenced and the nature in which it is formatted is superior to that adopted previously in Barry's manuscript. There are many instances where the referencing could be more up to date and consistent. There are, for example, instances where the year has been omitted from the reference details. The other major area that has been ignored is the role of physical enhancement in transdermal delivery. Many advances have been made since Barry's book but there is little mention of iontophoresis, sonophoresis and the more recent techniques such as electroporation and microneedles.

Overall this is an important text, albeit rather expensive, that should find a place on the shelves of pharmaceutical scientists whose major interest in percutaneous absorption.

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Methods of Tissue Engineering. Anthony Atala and Robert P. Lanza, Eds., Academic Press, San Diego, California, 2002. xli, 1285 pp., illustrations. $149.95.

Tissue engineering is based on novel combinations of cells, acellular biomaterials, and drugs. The combinations can be designed, specified, fabricated, and delivered simultaneously or sequentially as therapeutic agents. This book describes the tools, experimental protocols, detailed descriptions, and know-how's in this interdisciplinary field of tissue engineering.

In the first section, *Methods for Cell and Tissue Culture*, general directions as well as specific procedures are provided for cultivation of cells and tissues. After describing the general procedures for the cultivation of cells and tissues (Chapters 1–8), extensive reviews were made on the cell culture from various tissues. Normal epithelial cells will not survive for long and will not function properly unless epithelial cell and appropriate mesenchymal cells are cocultured. From this aspect of epithelial-mesenchymal relationship, several chapters are devoted to the culture of epithelial and mesenchymal cells (Chapters 9–28). There are chapters on the cultures of neuroectodermal and gonad cells (Chapters 29–32). Recently, the regenerative potential of stem cells has been under intense investigation. Tissue replacement in the body takes place by two mechanisms. One is the replacement of differentiated cells by newly generated populations derived from residual cycling stem cell. Blood cells are a typical example for this kind of regeneration. The second mechanism is the self-repair of differentiated functioning cells, preserving their proliferative activity. Hepatocyte, endothelial cells, smooth muscle cells, keratinocytes, and fibroblasts are considered to possess this ability. Stem cell culture and its characteristics are reviewed in Chapters 33–41.

In the second section, *Methods for Cell Delivery Vehicles*, detailed descriptions of polymers and methods for creating polymeric cell delivery vehicle are provided. Polymers for cell delivery vehicles can be either synthetic or naturally occurring. Synthetic polymers have received considerable attention for cell delivery and have shown promise in animal studies and some early human clinical trials because of their predictable and reproducible mechanical and physical properties. However, synthetic polymers tend to elicit a foreign material type of response in the host. As an alternative for solving this type of difficulty, natural polymers are being investigated as candidate materials. From this aspect, polymers in this section are classified into natural and synthetic polymers. In Chapters 42–47, the modification of natural polymers is focused to propose a suitable system for cell delivery. Collagen, albumin, hyaluronic acid, fibrinogen-fibrin, sodium alginate and chitosan are reviewed as candidate materials. In Chapters 48–57, detailed synthetic routes of synthetic polymers are introduced and prepared polymers such as aliphatic carbonate-based polymers, dioxanone-based polymers, polyphosphazene, poly(anhydride), poly(ortho esters), poly(amino acids), poly (propylene fumarate) and poly(N-isopropylacrylamide) are characterized for cell delivery vehicle. The aforementioned polymers were used in introducing various methods for creating scaffolds upon which cells may grow and flourish. As a simple method for fabricating construct for tissue engineering, the solvent casting method is introduced in Chapter 58. With proper selection of solvent and consideration on the polymer stability and cell toxicity, this method can provide the scaffold without using any special instruments. For the treatment of serious and disabling human conditions, encapsulated cell therapy has been developed based on the membrane technology. The method that provides the membrane with the desired combination of immunoisolation and product delivery rate is introduced in Chapter 59. Freeze-drying has been widely used to dry the various nutrients and proteins keeping their activities. This excellent property has been utilized and introduced in the preparation of the scaffolds containing the protein-based growth and differentiation factors at the time of processing (Chapter 60).

As an alternative to polymeric scaffolds, polymer-ceramic composite foams have been investigated. Three different methods are described for creating a porous, interconnected composite scaffolds of PLGA-hydroxyapartitie: a polymer-ceramic film formed by solvent casting, polymer-ceramic constructs synthesized by a solvent aggregation method, and polymer-ceramic constructs synthesized by the gel-microsphere method (Chapter 61). Several protocols for fabricating scaffolds related to different phase separation processes are introduced in Chapter 62. By proper selection of the method from solid-liquid phase separation, thermally induced liquid-liquid phase separation, and thermally induced gelation, various types of scaffolds can be prepared. Chapter 63 describes a simple method of scaffold formation by polymerization using poly (2-hydroxyethyl methacrylate) as an example. Because of solubility transition during the polymerization resulting in bicontinuous structure of polymer and solvent, the leaching process of porogen is not required. Gas foam process is applied to form highly porous polymeric scaffolds without use of high temperatures and organic solvents. This enables incorporation of large bioactive molecules in the scaffolds maintaining their activity, as presented in Chapter 64. For the better understanding of cell-polymer interactions in the design of scaffolds, the cell-synthetic polymer surface interactions are reviewed in Chapter 65–67. The microencapsulation methods, commonly used for preparation of

cell delivery vehicles, are reviewed in Chapters 68–76. The microencapsulation technologies are introduced with various capsule materials such as agarose-PSSA, sodium alginate, alginate-poly(l-lysine), alginate-polylysine-polyethyleneimine-protamine sulfate-heparin, glycosaminoglycans-chitosan, polyacrylate, and poly(vinyl alcohol).

The third section, *Methods for Engineering Cells and Tissues*, summarizes the remarkable progresses made to date in creating functional organ. Breast reconstruction is one of the most common reconstruction procedures. Reconstructing breast entirely on tissue engineering avoid the conventional problems. Various methods for breast reconstruction are described in Chapter 78. There are chapters on the creation of small blood vessels, and the growth of cardiac muscle, valves, and arteries. There are many methods for engineering these implants, but the fundamental concept that ties them together is their integration of a living (cellular) component into the construct. Various engineering methodologies from a variety of biomaterial scaffolds have been described in Chapters 79–82. Although a large number of tissues can be targets of tissue engineering, very few studies have been devoted to creating cornea, sections of the gastrointestinal tract, liver, and kidney due their complexity. Several chapters are devoted to describe the tissue engineering of these organs. (Chapters 83–87). Progress has been particularly remarkable for the urogenital tract. Structures created for repair of the urethra, penis, testes, and vagina have been described in Chapters 90–92. Chapters 93–108 review rebuilding phalanges of the hand and other joints as well as various methods for regeneration of the nerve system including procedures to regenerate spinal cord, peripheral nerves and parts of the brain.

This book is prepared for students in their early stages of learning tissue engineering as well as for advanced scientists in the life science field. This book serves as a guidebook for the next generation of scientists seeking more fundamental understanding on tissue engineering.

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Computational Methods for Protein Folding, Advances in Chemical Physics Series, Vol. 120. Richard A. Friesner, Ed., John Wiley & Sons, Inc., New York, New York, 2002. xiii, 528 pp., illustrations. $175.00.

How proteins, or sequences of the maximum 20 naturally occurring amino acids, fold into their specific "native" states, in which the biologic functionalities are carried out, has been imposing a very challenging task for scientists in various fields. Deciphering the extraordinary self-assembly ability of proteins requires not only experimental methods to obtain the high-resolution 3D structures, but also computational means to correlate fundamental atomic interactions with unique conformations in the native state. Because of the recent bloom of genomics and proteomics, hundreds of thousands of protein sequences have been identified. This is transforming the drug discovery and delivery to the "target-rich" scenario as the biologic functions of the proteins are being discovered. To accurately predict the protein structure from its sequence, without any doubt, is imperatively demanded. This book illustrates the state of the art of computational approaches and provides an excellent resource for the protein folding study.

Compiled with eight essays by the leading experts in the area, this book reports these researchers' own research and results in great details. One chapter discusses the simplest model for the protein folding, the lattice model, and how to apply it to model the folding kinetics. Another chapter shows a threading approach where the query sequence is matched to a library of template structures. These two approaches apparently rely on known structures that have been solved. Two more papers, in addition, are focused on how to apply the information from analyzing solved structures to the folding study, including the knowledge-based and statistical techniques. The third method, which is covered by the remaining four chapters, predicts the protein structure from a random conformation without direct reference to known protein structures. Referred to as the *ab initio* prediction, this kind of method searches the global minimum (i.e., the native state) from a protein's energy landscape. This requires efficient conformation searching schemes and accurate potential functions. One chapter discusses efficient sampling algorithms and two chapters show the development and application of potential energies that are derived from a combination of both empirical analysis and physical chemical principles. The last chapter goes beyond and uses an all-atom potential and a continuous salvation model for the structure prediction.

This book is well balanced. It covers a broad spectrum of currently developed methods, from the simple lattice model to the knowledge-based and atomic-level approaches. With a total of 528 pages and 8 chapters, this book demonstrates the current efforts to address the two key aspects of the protein folding study: conformation search and potential energy expression. It is well written and very informative. Needless to say, the protein structure prediction is still far away from maturing and many obstacles need to be overcome. Hence, this book is a must for those who start working in the protein structure prediction and a valuable reference for those who work in the drug discovery and delivery fields.

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Filtration in the Biopharmaceutical Industry. Theodore H. Meltzer and Maik W. Jornitz, Eds., Marcel Dekker, Inc., New York, New York, 1998. xiv, 933 pp., illustrations. $225.00.

This book is a major update of the original book published in 1987 titled *Filtration in the Pharmaceutical Industry*. The work contains twenty-nine well-referenced chapters, and is divided into five parts: Types of Filters, Filter Character-

ization, Utilitarian Considerations, Applications, and Regulatory Considerations. Theory is firmly balanced with application, laboratory technique aligned with quality and compliance, and regulatory requirements are stressed throughout. The stated goal of the editors, Theodore Meltzer and Maik Jornitz, was to document technical advances in the field, including those relative to biotechnology derived products. For example, virus removal and protein adsorption to microporous membranes were not routine aspects of drug development and manufacturing in 1987. The resulting work is a significant achievement documenting scientific advancements from around the world into a cohesive, well-edited volume.

Part I, Types of Filters, includes chapters on filter aids, polytetrafluoroethylene membrane technology, charge-modified membranes, prefilter construction, and an excellent discussion of cartridge filters by Peter Soelkner and Juergen Rupp.

Part II, Filter Characteristics, contains chapters on extractibles and filter compatability, quality assurance, and a very detailed review of pore sizes and bubble point theory contributed by Oscar Reif.

Part III, Utilitarian Considerations, includes chapters on bacterial biofilms, filtrative particle removal from liquids, integrity testing, filter sizing, and filter housings.

Part IV, Applications, includes chapters on crossflow filtration, protein adsorption to membranes, air and gas filtration, sterility testing using membrane filtration, and prefiltration technology. Wayne Olson contributed a particularly informative chapter on filtration of blood products.

Part V, Regulatory Considerations, includes an excellent chapter by Jornitz and Meltzer on validation of filtrative sterilization. This chapter compliments a superb chapter on the same subject by Rich Levy, Michael Phillips, and Herbert Lutz in Part IV.

In conclusion, the reviewer regards this book as an essential reference for those developing and utilizing filtration technology in the biopharmaceutical industry.

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Pharmaceutical Process Scale-Up. Michael Levin, Ed., Marcel Dekker, Inc., New York, New York, 2002. xvi, 566 pp, illustrations. $195.00.

Imagine that your next assignment involves the scale-up of a pharmaceutical process from a 10-L batch to a 300-L batch. Before you begin to panic take a look at this book. The strengths of the text include comprehensive coverage of many of the "significant" aspects of pharmaceutical scale-up, realistic case studies for nearly each process, and extensive reference lists. Potential areas of concern and practical solutions are presented through the eyes and experiences of experts from industry and academia. The index of the book is adequate, but in my opinion should have been more fully expanded to aid the reader in locating specific information without thumbing through several pages. In addition, there is some redundancy between chapters that should have been edited. The text caters to a broad audience including formulators, process engineers, technology transfer scientists, and individuals involved in product globalization.

The text begins with a discussion on the theory and application of dimensional analysis in pharmaceutical scale-up and is presented by Marko Zlokarnik. The chapter includes a comprehensive introduction to the subject and several examples to illustrate its applicability. The essentials of dimensional analysis are presented to help the reader determine which variables are relevant and which are not. Igor Gorsky discusses parenteral drug scale-up through the use of geometric similarity and dimensionless number methods, but favors the scale-of-agitation approach. Marco Cacciuttolo and coworkers present the following chapter on the scale-up of biotechnology-derived products. The chapter is composed of three sections that include discussions on the current technologies used in the manufacture of these commercial products and practical approaches to process design and scale-up strategies.

The remaining chapters of the text are dedicated to the scale-up of nonparenteral pharmaceuticals with the majority of the discussion devoted to Scale-Up and Post Approval Changes (SUPAC) in solid dosage forms. The arrangement of the chapters follows the logical progression of solid dosage form development. The subject of batch size increase in dry blending and mixing is co-authored by Albert Alexander and Fernando Muzzio. The chapter contains a comprehensive background on the current understanding of granular mixing, which includes a discussion of convection, dispersion, and shear within tumbling blenders. It concludes with a review of preliminary experimental results on how particle velocity may be a key aspect in determining segregation dynamics in twin-shell blenders. In the next chapter, James Prescott presents an introduction and comprehensive discussion on several key aspects of powder handling and flow properties such as cohesive strength, wall friction, and bulk density. In addition, sifting, air entrainment, and particle entrainment within blends are discussed and specific tests to identify segregation at the laboratory and production scale are considered. A discussion on blend sampling at scale would have been a useful addition. In chapter six, Hans Leuenberger discusses the use of dimensional analysis to determine the dimensionless groups within the fluid bed granulation process and ultimately to identify the scale-up invariants. Dilip Parikh authors the chapter on batch size increase in fluid bed granulation. He identifies the key process variables for fluid bed granulation, organizes them into three categories, and discusses each.

Chapter 8 is divided into three sections that are devoted to the scale-up of the tableting process. The first section is authored by Joseph Schwartz and provides the reader with a sound understanding of the basics of the tableting process. The physiochemical properties of the material to be compacted and the mechanical properties of the tablet press are discussed. Walter Strathy and Adolfo Gomez co-authored the second section, which contains two interesting case studies that involve blend-feed segregation and die cracking. The third section of the chapter is prepared by Michael Levin and Marko Zlokarnik and builds on the theories of dimensional analysis presented in Chapters 1 and 2 as they pertain to the tableting process. Experimental data is presented for the compaction of a viscoelastic material and a brittle material

and the observed values are compared to the predicted values, which were determined via dimensional analysis.

Following the natural progression of nonparenteral solid dosage form manufacture, the next chapter features a discussion by Stuart Porter on the scale-up of film coating. He suggests that scale-up of a film coating process should be done using a design of experiments and provides the reader with a list of critical operating parameters for the pan coating process. Furthermore, there is an interesting and relevant comparison of Schlick and Spray System nozzles. In addition to the pan-coating process, key concepts of the fluid-bed process are also discussed. The last chapter, authored by Ajaz Hussain, illustrates the value of establishing specifications for qualifying manufacture changes. The chapter is a compilation of discussions from various workshops and within the literature on SUPAC. Through an easy to follow example of a capsule product scale-up, he illustrates how the SUPAC-IR guidance defines the level of change and what control tests and documentation would be required for the change.

The appendices are quite extensive and are specifically targeted for the pharmaceutical industry as a reference manual for the regulatory concerns governing SUPAC. Regulations governing immediate release, modified release, extended release, and nonsterile semisolids dosage forms are highlighted. Regulatory issues regarding changes to an approved NDA or ANDA are also presented. The last section discusses the process of obtaining a waiver of BA/BE for immediate release dosage forms based on the biopharmaceutics classification system.

In summary, process scale-up is a "fascinating and vital part of the pharmaceutical industry." Michael Levin's text will not provide all the answers, but it will provide an understanding of the complexities associated with transferring pharmaceutical processes from lab scale to pilot plant to production scale. This understanding will then need to be fortified with hands-on experience.

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Books Received

Biomaterials

Polymeric Biomaterials. Second Edition, Revised and Expanded, Severian Dumitriu, Ed., Marcel Dekker, Inc., New York, New York, 2002. xiv, 1168 pp., illustrations. $275.00.

Safety Evaluation of Medical Devices, 2nd Ed., Shayne Cox Gad, Marcel Dekker, Inc., New York, New York, 2002. xii, 558 pp., illustrations. $195.00.

Handbook of Porous Media, Kambiz Vafai, Ed., Marcel Dekker, Inc., New York, New York, 2000. xvii, 908 pp., illustrations. $235.00.

Pharmaceutics & Pharmacology

Pharmaceutical Excipients 2001, Single-User Windows Version 2.0, Ray C. Rowe, Paul J. Sheskey, and Paul J. Weller, American Pharmaceutical Association and Pharmaceutical Press, Washington, DC, 2001. CD-ROM. $299.95.

Design and Analysis of Bioavailability and Bioequivalence Studies, 2nd Edn., Revised and Expanded, Shein-Chung Chow and Jen-pei Liu, Eds., Marcel Dekker, Inc., New York, New York, 2002. xii, 584 pp., illustrations. $195.00.

Drug Benefits and Risks. International Textbook of Clinical Pharmacology, Chris J. van Boxtel, Budiono Santoso, and I. Ralph Edwards, Eds., John Wiley & Sons, Inc., New York, New York, 2001. xv, 717pp., illustrations. $160.00.

Textbook of Biochemistry with Clinical Correlations, 5th Edn., Thomas M. Delvin, Ed., Wiley-Liss, A John Wiley & Sons, Inc., New York, New York, 2002. xxiv, 1216pp., illustrations. $99.94.

Polymer Chemistry & Organic Chemistry

Preparative Methods of Polymer Chemistry, 3rd Ed., Waybe R. Sorenson, Fred Sweeny, and Tod W. Campbell, John Wiley & Sons, Inc., New York, New York, 2001. xvi, 488 pp, illustrations. $79.95.

Polymer Solutions, An Introduction To Physical Properties, Iwao Teraoka, John Wiley & Sons, Inc., New York New York, 2002. xv, 338 pp., illustrations. $79.95.

Polymer Modification, Principles, Techniques, and Applications, John J. Meister, Ed., Marcel Dekker, Inc., New York, New York, 2000. x, 914 pp., illustrations. $235.00.

The Pyrazines, Supplement I, D.J. Brown, An Interscience Publication, John Wiley & Sons, Inc., New York, New York, 2002. xvi, 557pp., illustrations. $425.00.

Proteomics

Introduction to Proteomics. Tools for the New Biology, Daniel C. Liebler, Humana Press Inc., Totowa, New Jersey, 2002. ix, 198 pp., illustrations. $24.50.

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